ANALGESIC ANTI-INFLAMMATORY AND HEPATOPROTECTIVE ACTIVITIES OF AERIAL PARTS OF *FLACOURTIA SEPIARIA* ROXB

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Abstract— The present study was carried out to investigate the *in vivo* acute toxicity study, analgesic anti-inflammatory and hepatoprotective activities of various extracts of the aerial parts of *Flacourtia sepiaria* Roxb which belongs to the family of Flacourtiaceae. *Flacourtia sepiaria* is traditionally used as an antidote for snake poisoning, rheumatoid arthritis, gout and kidney diseases. The methanolic extract was found to be very safe up to 2000mg/kg body weight by acute toxicity model study as per the OECD guidelines 423. The methanol extract showed significant anti-nociceptive (analgesic) anti-inflammatory and hepatoprotective activities in a dose dependent manner. The methanol extract at the dose of 400 mg/kg exhibited significant anti-nociceptive anti- inflammatory and hepatoprotective activity. This activity can be attributed to the phenolic and flavonoid content in the methanol extract.

Keywords— *Flacourtia Sepiaria*, Acute Toxicity, Analgesic, Anti-Inflammatory, Hepatoprotective.

I. INTRODUCTION

Medicinal plants continue to play a vital role in the healthcare system of large proportions of world's population. Over the past decade, herbal medicine has become a topic of global importance, making an impact on both world health and international trade [1]. India is one of the world's twelve leading biodiversity centers with the presence of over 45,000 different plant species. India's diversity is unmatched due to the presence of sixteen different agro climatic zones, ten vegetation zones, twenty-five biotic provinces and four hundred and twenty-six biomes.

Analgesics are primary need of patients to get rid of any kind of pain. The pain is one of the basic symptoms of almost all human ailments which are a sensorial modality and primary protection. Analgesics only relieve pain in a particular complaint without affecting its cause[2]. The most eminent analgesics including opiates and NSAIDs are not helpful in all cases due to their adverse effects. Consequently, the new compounds with potent painkiller action and no side effects are being required to investigate. Beside pain, the inflammation involves a complex array of enzyme activation, mediator release, fluid extravasations, cell migration, tissue breakdown and repair which are aimed at host defense and usually activated in most disease conditions[3]. At present, the natural analgesics and anti-inflammatory of plant origin are being appreciated due to possible toxicity of synthetic drugs.

Inflammation is essentially the process by which the body's white blood cells attack bacteria and viruses. White blood cells, when detecting a pathogen, leave the blood vessel and release chemicals directed at the foreign object. In some cases, the immune system triggers an inflammatory response even in the absence of a pathogen. Anti-inflammatory refers to the property of a substance or treatment that reduces inflammation. Anti-inflammatory drugs make up about half of analgesics, remedying pain by reducing inflammation as opposed to opioids which affect the brain. All the conventional NSAID's like aspirin, diclofenac, ibuprofen, indomethacin inhibit both COX-I and COX-II. Thus provide powerful relief from pain and inflammation.

Liver is one of the largest organs in human body and the chief site for intense metabolism and excretion. So it has a surprising role in the maintenance, performance and regulating homeostasis of the body. It is involved with almost all the biochemical pathways to growth, fight against disease, nutrient supply, energy provision and reproduction[4]. The major functions of the liver are carbohydrate, protein and fat metabolism, detoxification, secretion of bile and storage of vitamin. Thus to maintain a healthy liver is a crucial factor for overall health and well being. But it is continuously exposed to environmental toxins and abused by poor drug habits and alcohol and prescribed over the counter drug which can eventually lead to various liver ailments like hepatitis, cirrhosis and alcoholic liver disease[5].

Thus by considering the above pros and cons related to the use of natural products we have embarked a research programme aimed at evaluating the plant *Flacourtia sepiaria* for its analgesic, anti-inflammatory and hepatoprotective properties.

Flacourtia sepiaria belonging to the family of Flacourtiaceae is a medium sized tree widely distributed in the dry jungles of Bengal, Bihar, Orissa and all districts of the Madras presidency. An infusion of the leaves is given in case of snake bites and its bark triturated with sesame oil is used as a liniment in rheumatism and gout. The ashes of root

are also given in kidney diseases[6]. It has also been proved to posses antimicrobial activity[7].

Flacourtia sepiaria (Flacourtiaceae) is the most useful traditional medicinal plant in India. Although there is no such Phytopharmacological activities has been carried out but, still it is considered as a valuable source of unique natural products for development of medicines and targeting against various diseases. Each part of its allied species i.e., (leaves, bark, stem, fruits, root and even whole plant) of the *Flacourtia indica* has demonstrated several pharmacological activities. So its quantification of the individual phytoconstituents as well as pharmacological profile based on *in vitro, in vivo* studies has been investigated.

II. AIM AND OBJECTIVE OF THE PRESENT STUDY

In the present study we have chosen the plant *Flacourtia sepiaria* Roxb of family Flacourtiaceae traditionally used in the treatment of rheumatoid arthritis, inflammation, gout, helminthic infestations, kidney diseases and also as an antidote to snake bite .

Based on the extensive medicinal claims of *Flacourtia sepiaria* Roxb the current research work was carried out in order to scientifically evaluate the folklore claims and to explore the unexplored phytochemical constituents.

The literature reveals that there are no previous reports with regard to investigate the anti-nociceptive, anti-inflammatory and anti-inflammatory activity of the various extracts of the plant. So the present study was planned to evaluate analgesic, anti-inflammatory activities including acute toxicity study.

III. MATERIALS AND METHODS

Plant material: *Flacourtia sepiaria* Roxb. The aerial parts and leaves of *Flacourtia sepiaria* were collected from Tirunelveli district, Tamilnadu, India during the month of March 2011. The plant was identified and authenticated by Mr. Chelladurai, Research Officer-Botany, Central Council for Research in Ayurveda and Siddha, Government of India (Ref No:-NCP/CH/PS02). All the drugs and chemicals used for the work were purchased commercially and were of analytical grade. Instruments used were: Digital Balance (Sartorius Ltd, USA), Eppendorff minispin, Mechanical shaker (Hitachi Ltd., Tokyo, Japan), Shimadzu UV-1601 UV-Vis spectrophotometer.

Preparation of the extracts of aerial parts of *Flacourtia sepiaria*

The aerial parts of *F. sepiaria* were collected, shade dried for 3 weeks, powdered mechanically and sieved through No. 20 mesh sieve. About 800g of the powdered aerial part was first defatted with petroleum ether (PEF, 60º-80ºC) and then consecutively extracted with ethyl acetate (EAEF) and methanol (MEF) by soxhlet extraction (order of increasing polarity). The crude extracts were concentrated by using rotary vacuum evaporator and dried at room temperature. The extract obtained with each solvent was weighed and the percentage yield was calculated in terms of dried weight of the plant material.

Acute toxicity study

Toxicity studies were conducted as per internationally accepted protocol drawn under OECD guidelines 423 in Swiss albino mice.

In-vivo anti-inflammatory activity: Carrageenan-induced paw edema in rats

Wister rats of either sex with a body weight between 180-220 g were used. The animals were fasted for 18 hours prior to the experiment. Animals were divided into six groups of six animals each. Group I received normal saline (0.9%) and served as control. Group II received diclofenac sodium 50 mg/kg b.w i.p and served as standard. Group III, IV, V and VI received the MEF and EAEF extract respectively at dose of 200 mg/kg and 400 mg/kg b.w orally. One hour after oral administration, an injection of 0.1ml of carrageenan (1% carrageenan suspended in 0.9% NaCl) was made into the right hind limb of each rat under the sub plantar aponeurosis. Measurement of paw volume was done by means of volume displacement technique using plethysmometer (Ugo Basile Italy) immediately after carrageenan injection and after 6 hours. The results were tabulated by percentage of inhibition[8].

$$\text{Percentage inhibition} = \frac{(vt-vo)control - (vt-vo)treated}{(vt-vo)control} \times 100$$

Vt is the average volume for each group after treatment and Vo is the average volume for each group before treatment.

Anti-nociceptive activity

Writhing test in mice

The abdominal writhing response to the acetic acid (1%, 10 ml/kg i.p) administration involves contractions of the hind limbs. The number of abdominal writhing was recorded for a period of 10 min, starting 5 min after the administration [9]. For the writhing tests, mice received acetic acid injection 30 min after receiving their respective treatment. Group I was pretreated with saline solution (0.9%; 0.1 ml/10 g b.w, i.p). Group II was pretreated with diclofenac (5mg/kg b.w, i.p).Group III, IV, V, VI were treated with MEF and EAEF extracts (200 mg/kg b.w orally 400 mg/kg b.w, orally) respectively. Antinociception was calculated as percentage of inhibition of writhing constrictions.

Percentage inhibition = $\frac{(control\ group - test\ group)}{(control\ group)}$ X 100

Tail immersion test in rats

Wister rats of either sex with a body weight between 180-220 g were used. The animals were fasted for 18 hours prior to the experiment. Animals were divided into six groups of six animals each. The tail immersion test basically involves the measure of the response latency of rats to a nociceptive stimulus. This involves introducing 3 cm of the rat's tail in hot water at a temperature of 55 ± 0.5°C. Within a few minutes, the rats reacted by withdrawing the tail. The reaction time was recorded with a stopwatch. The animals were treated by MEF and EAEF extracts (200 and 400 mg/kg), or water (vehicle) or standard drug (morphine, 10 mg/kg), 30min before the immersion of the tail. The time reaction is taken at 30, 60, 90 and 120 min after administration of different preparations [10].

Hepatoprotective activity

Treatment protocol

The acclimatized animals were divided into 5 groups of each 6 animals, designated as

Group 1: Served as normal control and receive normal diet and water.

Group 2: Toxic control received 400 mg/kg i.p D-galactosamine for 21 days.

Group 3: Standard control received 25 mg/kg of silymarin orally for 21 days.

Group 4: Served as a treatment control group and was administered methanolic extract of *Flacourtia sepiaria* Roxb (MEF) at a dose of 200mg/kg through orally for 21days

Group 5: Served as a treatment control group and was administered methanolic extract of *Flacourtia sepiaria* Roxb (MEF) at a dose of 400mg/kg through orally for 21 days.

Biochemical Analysis:

On the 22nd day, after 24 hrs of galactosamine administration, animals in all the groups were humanely sacrificed using ketamine HCl and 4ml of blood was withdrawn by cardiac puncture and allowed to clot for 30min at room temperature. The serum was separated by using refrigerated centrifuge and used for the assay of marker enzymes viz AST, ALT, ALP, TP, TB and LDH. The livers were dissected out immediately, washed with ice-cold saline and 10% homogenates in phosphate buffer solution (pH 7.4) were prepared. Liver homogenate was used for the assay of lipid per oxidation (LPO) while some fraction of homogenates were centrifuged at 7000rpm for 10 min at 4° C using refrigerated centrifuge, and the supernatants were used for the assay of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx). Some portion of liver from each group was aseptically excused and stored in 10% formalin for histopathological studies [11].

IV. RESULTS AND DISCUSSIONS

Acute toxicity study

The LD_{50} of the extracts when administered orally to mice was found to be 2000 mg kg^{-1} according to OECD guidelines 423.

During the acute toxicity study, the methanolic extract was administered orally and animals were observed for mortality, changes in the autonomic nervous system, central nervous system and behavioral responses. There was no mortality observed even at 2000mg/kg for the extract. All the animals were found to be normal and there were no gross behavioral changes till the end of the observation period. This observation revealed that the methanolic extract of the aerial parts was found to be very safe up to 2000mg/kg of body weight known as maximum tolerated dose (MTD) by acute toxicity model study as per OECD guidelines 423. Hence from this 1/10th and 1/5th of MTD was selected and the effective doses were fixed as 200 and 400 mg/kg for the further pharmacological studies.

Anti-inflammatory activity: Carrageenan-induced paw edema in rats

Table 1: Effect of control (saline), diclofenac sodium, MEF and EAEF on paw edema induced by carrageenan in rat.

Treatment	Dose (mg kg^{-1})	Volume of paw edema (mL)	Inhibition (%)
Group I Normal saline	-	5.60±0.98	-
Group II Diclofenac sodium	50	1.80±0.32	67.85%*a
Group III MEF	200	2.10±0.52	62.50%*a
Group IV MEF	400	1.96±0.60	65.00%*a
Group V EAEF	200	2.72±0.32	51.42%*a
Group VI EAEF	400	2.51±0.44	55.17%*a

* Data are expressed as Mean ± S.E.M. *Data were analyzed by one way ANOVA followed by Newman's keul's multiple range tests, to determine the significance of the difference between the control group and rats treated with the test compounds.

*a Values were significantly different from normal control at P< 0.01.

The treatment with crude extracts, MEF and EAEF (200 and 400 mg kg^{-1}), as well as diclofenac (50 mg kg^{-1}) inhibited significantly (p< 0.01) the carrageenan induced rat paw edema formation which was measured at the sixth hour of the experiment (Table 1). The results were significant in comparison to the control. Carrageenan induced edema has been commonly used as an experimental animal model for acute inflammation and is believed to be biphasic[12]. The early phase (1-2 h) of the carrageenan model is mainly mediated by histamine, serotonin and increased synthesis of prostaglandins in the damaged tissue surroundings. The late phase is sustained by prostaglandin release and mediated by

bradykinin, leukotrienes, polymorphonuclear cells, and prostaglandins produced by tissue macrophages [13]. Since the extract significantly inhibited paw edema induced by carrageenan in the second phase, this finding suggests a possible inhibition of cyclooxygenase synthesis by the extract and this effect is similar to that produced by nonsteroidal anti-inflammatory drugs such as diclofenac sodium, whose mechanism of action is inhibition of the cyclooxygenase enzyme[3].

Flavonoids, steroids and saponins are well known for their anti-inflammatory properties due to their inhibitory effects on enzymes involved in the production of the chemical mediator of inflammation [14]. The ability of flavonoids and sterols like β-sitosterol to inhibit eicosanoid biosynthesis has been documented [15]. Eicosanoids, such as prostaglandins, are involved in various immunological responses and are the end products of the cyclooxygenase and lipoxygenase pathways [16,17]. Further, flavonoids are able to inhibit neutrophils degranulation and thereby decrease the release of arachidonic acid[18].

Anti-nociceptive activity

Abdominal writhing test in mice

Table 2: Effect of control (saline), diclofenac sodium, MEF and EAEF on acetic acid induced writhing reflux in mice.

Treatment	Dose (mg kg^{-1})	No. of writhing (±SEM)	Inhibition (%)
Group I Normal saline	-	38.2±4.6	-
Group II Diclofenac sodium	50	6.4±0.9	83.24%**
Group III MEF	200	13.2±1.6	65.44%**
Group IV MEF	400	12.4±1.2	67.53%**
Group V EAEF	200	17.1±1.6	55.23%**
Group VI EAEF	400	15.9±1.4	58.37%**

Values were find out by using one-way ANOVA followed by Newman's keuls multiple range tests. ** Values were considered significant at P< 0.001.

The results presented in table 2 shows that the MEF and EAEF (200 and 400 mg kg^{-1}) of *F. sepiaria* inhibited significantly (p< 0.001) the acetic acid induced abdominal constrictions. The protective effect of the extracts reached a maximum inhibition of 67.53% for MEF and 58.37% for EAEF at the dose of 400 mg kg^{-1}. Diclofenac sodium (standard) was more potent than the antinociceptive dose of the extract, with percentage protection of 83.24%. The acetic acid-induced writhing model represents pain sensation by triggering localized inflammatory response. Such pain stimulus leads to the release of free arachidonic acid from the tissue phospholipid [19]. The acetic acid induced writhing response is a sensitive procedure to evaluate peripherally acting analgesics. The response is thought to be mediated by peritoneal mast cells [20], acid sensing ion channels [21], and the prostaglandin pathways [22]. The MEF and EAEF inhibited acetic acid induced writhing indicating its peripheral analgesic activity.

Tail immersion test in mice

Table 3**:** Effect of control (saline), morphine, MEF and EAEF on tail withdrawal reflex induced by tail immersion in rats.

Groups	Dose (mg kg^{-1})	30 min (±SEM)	60min (±SEM)	90 min (±SEM)	120 min (±SEM)
Group I Normal saline	-	1.3 ± 0.1	1.4 ± 0.2	1.8 ± 0.2	2.5 ± 0.2
Group II Morphine	50	6.4 ± 0.8**	8.5 ± 0.9**	8.6 ± 0.8**	8.9 ± 0.9**
Group III MEF	200	5.9 ± 0.6 **	6.2 ± 0.7**	6.4 ± 0.6**	6.6 ± 0.8**
Group IV MEF	400	6.8 ± 0.7**	7.2 ± 0.9**	7.6 ± 1.0**	7.8 ± 1.3**
Group V EAEF	200	5.1 ± 0.8**	5.3 ± 1.4**	5.6 ± 0.6**	5.9 ± 0.2**
Group VI EAEF	400	5.7 ± 0.6**	6.0 ± 0.8**	6.2 ± 0.2**	6.5 ± 1.2**

Values were find out by using one-way ANOVA followed by Newman's keuls multiple range tests.
**** Values were considered significant at P< 0.001.**

Table 3 shows the effects of the methanol and ethyl acetate extract (200 and 400 mg kg^{-1}) in the tail immersion test in rats. A significant (p< 0.05) increase in the reaction time was observed in the tail immersion test in rats after 30, 60, 90 and 120 min when compared with the control. Morphine (standard) at dose of 10 mg kg^{-1} exhibited more potent activity at 30, 60, 90 and 120 min than the extracts. The brain and spinal cord play a major role in central pain mechanisms. The dorsal horn of the spinal cord is endowed with several neurotransmitters and receptors including substance P, somatostatin, neuropeptide Y, inhibitory amino acid, nitric oxide, endogenous opioids, and the monoamines which are the major targets for pain and inflammation [23]. The tail immersion test was considered to be selective to examine compounds acting through opioid receptor. Both the extracts increased pain threshold which means basal latency, which indicates that it may act *via* centrally mediated analgesic mechanism.

MEF showed highest analgesic activity in all the experimental model which may be due to its high flavonoid contents which are responsible for free radical scavenging activity, as these free radicals are involved during pain stimulation, and antioxidants showed reduction in such pain[24].The results of the present study have shown that the crude extract of the investigated plant exhibited very high anti-inflammatory and analgesic activities. These activities may be linked with the presence of polyphenolic compounds present in the extract.

Hepatoprotective activity

Table 4: Effect of methanolic extract of *Flacourtia sepiaria* and Silymarin pre-treatment on biochemical parameters of the rats intoxicated with D-Galactosamine.

Group. No.	TREATMENT DOSE (mg/Kg)	AST (IU/mL)	ALT (IU/mL)	ALP (IU/mL)	TP (gm/dl)	TB (mg/dl)	LDH (U/L)
I	Normal control 10ml/kg normal saline	80.70±3.95	48.45±2.44	64.30±2.12	6.20±0.70	0.48±0.15	212.40±6.52
II	Toxic control 25mg/kg D-galactosamine	306.22±8.35*a	325.30±7.75*a	295.20±6.30*a	3.40±0.30*a	1.22±0.30*a	356.30±7.20*a
III	Standard control Silymarin 25mg/kg	155.36±4.25*b	160.65±4.40*b	196.42±5.20*b	5.50±0.60*b	0.60±0.15*b	250.20±6.75*b
IV	Treatment control MEF 200mg/kg	240.60±6.62*b	222.70±5.20*b	268.30±5.75*b	4.58±0.42*b	0.90±0.18*b	285.18±7.02*b
V	Treatment control MEF 400mg/kg	225.55±5.68*b	205.50±5.05*b	252.30±5.30*b	4.75±0.48*b	0.82±0.16*b	262.20±6.80*b

- Values are expressed as Mean ± SEM.
- Values are found out by using one way ANOVA followed by Newmann keul's multiple range tests.
- *a – values are significantly different from normal control at P< 0.01.
- *b – values are significantly different from toxic control (G2) at p< 0.01.

Table 5: Effect of methanolic extract of *Flacourtia sepiaria* and silymarin pre-treatment on biochemical liver parameter in D-Galactosamine induced hepatotoxicity.

Group. No.	TREATMENT DOSE (mg/Kg)	SOD (U/mg) Protein	CATALASE (U/mg) Protein	GPx (U/mg) Protein	LIPID PEROXIDATION (nmoles OF MDA/g liver weight)
I	Normal control 10ml/kg Normal saline	9.12±0.86	0.195±0.06	10.8±0.90	106.76±4.06
II	Toxic control 25mg/kg D-galactosamine	2.60±0.12*a	0.012±0.01*a	2.60±0.14*a	160.82±7.92*a
III	Standard control Silymarin 25mg/kg	7.88±0.68*b	0.090±0.04*b	8.82±0.62*b	112.80±4.25*b
IV	Treatment control MEF 200mg/kg	7.22±0.60*b	0.078±0.02*b	7.60±0.45*b	136.42±4.84*b
V	Treatment control MEF 400mg/kg	7.52±0.64*b	0.084±0.03*b	8.25±0.55*b	128.30±4.48*b

- Values are expressed as Mean ± SEM.
- Values are find out by using one way ANOVA followed by Newmann keul's multiple range tests.
- *a – values are significantly different from normal control at P< 0.01.
- *b – values are significantly different from toxic control (G2) at p< 0.01.

Biochemical observations

Significant increase in (P<0.01) Serum Aspartate Transaminase (AST), Alanine Transaminase (ALT) , Alkaline phosphatase (ALP) , Total bilirubin (TB) and Lactate dehydrogenase and significant decrease in (P<0.01) Total protein levels were observed in animals treated with galactosamine 400mg/kg (Group II) as compared to normal control group (Group I).

Pretreatment with methanolic extract of *Flacourtia sepiaria* (MEF) at a dose 200mg/kg and 400mg/kg, orally for 21 days decreased the levels of above indices like AST, ALT , ALP, TB, LDH, and increased levels of TP significantly (P <0.01) in group IV and V.

Silymarin pretreatment produced significant decrease in (P< 0.01) serum AST, ALP, TB, LDH and significant increase in TP at (P< 0.01) in group III.

Biochemical observation in liver homogenate tissue

In liver homogenate, there was significant decrease in SOD, CAT and GPx levels and increase in LPO levels were observed in animals treated with galactosamine 400mg/kg (group II) as compared to normal control group (Group I).

Pretreatment with methanolic extract of *Flacourtia sepiaria* (MEF) at a dose 200mg and 400mg/kg, orally for 21 days increase the levels of above indices like SOD,CAT and GPx levels and decrease levels of LPO significantly (P<0.01) in group IV and V.

Silymarin pretreatment produced significant increase in (P< 0.01) Liver homogenate enzyme such as SOD,

CAT, GPx levels and decrease the levels of LPO significantly (P<0.01) in group III.

Histopathological Observations

Histology of liver sections of normal control animals (Group I) showed normal liver architecture which were brought out central vein, were preserved cytoplasm and prominent nucleus and nucleolus. The liver sections of galactosamine treated animals (Group II) showed hepatic cells with serum toxicity characterized by inflammatory cell collection, scattered inflammation across liver parenchyma, focal necrosis and swelling up of vascular endothelial cells. Silymarin (Group-III) exhibited protection from galactosamine induced changes in the liver.Pretreatment with methanolic extract of *Flacourtia sepiaria* (MEF) at a dose 200mg and 400mg/kg, (group IV and V) appeared to significantly prevent the galactosamine toxicity as revealed by the hepatic cells with were preserved cytoplasms. Pretreatment also caused marked decrease in inflammatory cells.

SUMMARY AND CONCLUSION

A scrutiny of the literatures revealed that the information by researchers available on this plant species regarding phytochemical, antioxidant and pharmacological activity was scarce. This study was structured for the screening of pharmacological activities and unexplored phytoconstituents in order to ascertain its folklore claims.

The extracts of *Flacourtia sepiaria* were evaluated for their *in vivo* analgesic and anti-inflammatory activities. Among these extracts, methanol extract was the most effective of all extracts it was selected for the screening of *in-vivo* pharmacological studies.

The *in-vivo* pharmacological activities basically included the screening of acute toxicity study, anti-nociceptive and anti-inflammatory activities of methanol extract of the aerial parts of *Flacourtia sepiaria* Roxb.

The methanolic extract was found to be very safe up to 2000mg/kg body weight by acute toxicity model study as per the OECD guidelines 423. The methanol extract showed significant anti-nociceptive, anti-inflammatory and hepatoprotective activities in a dose dependent manner. The methanol extract at the dose of 400 mg/kg exhibited significant hepatoprotective, anti-nociceptive and anti-inflammatory activity. This activity can be attributed to the phenolic and flavonoid content in the methanol extract.

The various pharmacological activities established by the test extract can be investigated further in future to get their meaningful extension in clinical use. The therapeutic activities were carried out scientifically and reported for the first time in this plant.

To conclude, the results of this thesis work provides, to the extent possible, a scientific basis to the traditional use of *Flacourtia sepiaria*. This scientific study revealed the efficacy of the drug and it would definitely have wide scope in future. Hence, *Flacourtia sepiaria* can be recommended therapeutically for the investigated medicinal claims. These observations will stimulate further research in the field of phytochemistry and also in the clinical application of phytochemical constituents of ***Flacourtia sepiaria Roxb.***

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